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The power of serum albumin levels in predicting mortality in critical patients

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ABSTRACT

Aims: Given the presence of comorbidities and critical illnesses in patients admitted to the intensive care unit (ICU), it is imperative to accurately forecast their prognosis and mortality in order to effectively plan and administer their therapies. Decreased serum albumin level is associated with adverse clinical outcomes. We designed this study to evaluate the prognostic value of decreased serum albumin level and its association with age in critically ill patients based on data obtained from the intensive care unit (ICU).

Methods: Data of patients followed between June 2022 and December 2023 in the Internal Medicine ICU of Akdeniz University Hospital were retrospectively reviewed. Albumin, C-reactive protein (CRP), Sequential Organ Failure Assessment (SOFA), and Acute Physiology and Chronic Health Evaluation II (APACHE-II) scores were documented within the initial 24 hours following admission to the ICU. Delta Albumin expression was used to express the changes between albumin values. The relationship between the obtained data and age was examined and compared between the surviving and deceased patient groups.

Results: 300 patients were included in the study. Albumin levels were significantly lower at admission compared to discharge in both the survival and deceased groups (both p<0.001). Changes in albumin levels were significantly associated with ICU mortality independently of age, gender, SOFA, and APACHE changes. Lower albumin levels were associated with worse survival (Hazard ratio: 0.80; 95% Confidence interval: 0.69-0.92; p=0.001).

Conclusion: Changes in albumin levels were significantly associated with ICU mortality independently of age, gender, SOFA, and APACHE changes.

Keywords: Intensive care, albumin level, mortality

INTRODUCTION

In humans, albumin constitutes the most abundant plasma protein, accounting for approximately 55-60% of the measured serum protein.[1] Unlike synthetic colloids, albumin binds reversibly to drugs, hormones, bilirubin, and metal ions, among other substances, affecting their metabolism in hypoalbuminemic critically ill patients.[2] The distrubiton of albumin in the body is variable and interesting. The initial approach in the pharmacokinetics of albumin involves the intercompartmental movement and the exchange between plasma and extravascular space, which is faster than metabolic changes.

Exchange rate between departments is assumed to be approximately 1 day, while the overall exchange rate is assumed to be approximately 25 days.[3] In this cycle, the kidneys account for around 6% of the clearance, the gastrointestinal system accounts for approximately 10%, and catabolism accounts for 84%, while the liver has a synthesis rate of 10.5 g/day for albumin.[4] The second approach is uncompartmental and assumes that the effective albumin concentration. in the metabolic region is equal to the plasma concentration.[5]

The synthesis rate of albumin is also significantly decreased in critically ill patients. Trauma, inflammation, or sepsis-induced acute phase response lead to an increase in gene transcription rates for positive acute phase proteins such as C-reactive protein, while they cause a decrease in albumin mRNA transcription and consequently synthesis rates.[6] A continuous inflammatory response in critical illness can lead to prolonged inhibition of albumin synthesis. Both interleukin-6 and tumor necrosis factor-alpha show gene transcription-reducing effects.[7] Scoring systems in critical care medicine aim to measure the severity of diseases and evaluate patient groups based on objective criteria.[8] The Acute Physiology and

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Chronic Health Evaluation II (APACHE-II) score, calculated using data collected within the first 24 hours of admission to the intensive care unit, predicts in-hospital mortality; an increase in the score is associated with increased mortality risk. The Sequential Organ Failure Assessment (SOFA) score evaluates disease-related organ failure and can be recalculated repeatedly during intensive care unit (ICU) stay to monitor disease progression. High values are associated with increased organ system failure (neurological, respiratory, cardiovascular, renal, hepatic, and hematological).[9]

Considering the comorbidities and critical conditions of patients admitted to the ICU, prognosis and mortality prediction, and accordingly the adjustment of treatments, are crucial for these patients. Moreover, it is believed that the results obtained from this and similar studies will provide significant benefits for improving the follow-up and treatment processes of critically ill elderly patients in future intensive care services, thus reducing morbidity and mortality rates.

This study aimed to identify and predict factors that influence the prognosis of patients during their ICU follow-ups.

METHODS

This study was conducted at the Internal Medicine Intensive Care Unit of Akdeniz University Hospital between June 2022 and December 2023. Prior to the study, approval was obtained from the Akdeniz University Medical Scientific Researches Ethics Committee (Date: 25.04.2024, Decision No: KAEK-274, Annex 1). The study was conducted in accordance with the principles outlined in the Helsinki Declaration.

Method of Sudy t

The research is a retrospective clinical study based on the collection of retrospective data. The study has an observational research nature.s

Scope of the Research

Patients followed in the Internal Medicine Intensive Care Unit of Akdeniz University, who were monitored for at least 24 hours in the intensive care unit, were included in the study. Patients who were referred to an external center during hospitalization, patients monitored in the postoperative intensive care unit, and patients for whom any of the study parameters could not be calculated (due to inability to perform necessary tests, data inadequacy) were excluded from the study. Patients who presented to the intensive care unit multiple times during the study period were only included in the study at their initial presentation.

Data Collection Methods

The necessary data for this study were obtained from intensive care patient follow-up records, hospital electronic database, physician daily observation notes, nurse observation notes, test results, and evaluations performed in the department where the patient was admitted. Retrospective demographic and clinical data were collected from all patients. Patients were classified as survivors or deceased based on the outcomes of their ICU stay.

The APACHE II score was compiled using the worst values of 12 acute physiological variables (temperature, blood pressure, heart rate, respiratory rate) obtained during the first 24 hours in the intensive care unit. Missing data were assumed to be normal. The SOFA score was compiled from arterial oxygen saturation, fraction of inspired oxygen, serum creatinine, total bilirubin, platelet count, detailed Glasgow Coma Scale (GCS) score, mean arterial pressure, and the use of vasopressors such as dopamine, dobutamine, adrenaline, and noradrenaline. The albumin values measured within the first 24 hours of admission to the intensive care unit were referred to as 'entry values,' while those measured within the last 24 hours before discharge from intensive care or before death were referred to as 'exit values.' ΔAlbumin values were defined to represent the change in albumin score obtained.

Statistical Analysis

The data obtained in the study were statistically analyzed using IBM SPSS Statistics 24.0 software (IBM Co., Armonk, NY, USA). Visual and statistical tests for normality were conducted. Categorical variables were expressed as number (n) and percentage (%), while continuous variables were expressed as median [interquartile range (IQR)] for normally distributed data, and as mean±standard deviation (SD) values otherwise. The Chi-square test was used to assess relationships between categorical variables. Student's t-test was used for comparing normally distributed numerical parameters between two independent groups, while the Mann-Whitney U test was used for comparing parameters that did not follow normal distribution. One-way analysis of variance (ANOVA) for repeated measurements was used for normally distributed data with homogeneous variances, and the Wilcoxon signed-rank test was used for non-normally distributed data. Cox regression analysis was conducted to evaluate factors affecting mortality risk, and model fit was assessed with the Concordance Index. A significance level of $p<0.05$ was accepted in the study for statistical significance.

RESULTS

A total of 300 patients who were admitted to the intensive care unit (ICU) and followed were included in the study.. The mean age of the deceased patients was 64.0±13.6 years, while the mean age of the surviving patients was 59.4±19.5 years, and the difference was found to be statistically significant (p=0.017). The distribution of gender was also statistically different between the two groups, with a significantly higher proportion of males among the deceased patients compared to the surviving patients (p=0.008). The burden of chronic diseases, regular medication use, and other basic characteristics were similar between the groups. The majority of deceased patients, accounting for 87.2%, were admitted from the ward, while this rate was seen to be 73.8% for surviving patients (p=0.005).

The median duration of ICU follow-up was significantly longer in deceased patients compared to surviving patients (p=0.002). The history of steroid use and the need for platelet replacement were significantly higher in deceased patients, but there was no significant difference between the groups

in terms of the need for erythrocyte replacement. He most common indication for ICU admission among both groups was acute respiratory failure. However, this indication was significantly more prevalent among deceased patients compared to those who survived (40.2% vs. 28.4%, p=0.035). Septicemia was identified as the second most common reason for ICU admission. A statistically significant difference was also observed between the survived and deceased groups, with septicemia occurring in 35.0% of deceased patients compared to 16.4% of survived patients (p<0.001).The need for Mechanical Ventilation (MV) was significantly higher in deceased patients in the intensive care unit (p<0.001). The basic and clinical characteristics of the patients are detailed in **Table 1**.

Table 1. Examination of basic and demographic characteristics of patients followed in the intensive care unit according to survival status

	Survival (n=183)	Deceased (n=117)	p
Age, years	59.4±19.5	64.0±13.6	0.017
Gender			
Female	86 (47.0%)	37 (31.6%)	0.008
Male	97 (53.0%)	80 (68.4%)	
Hospitalization in the ICU			
Sepsis	30 (16.4)	41 (35.0)	<0.001
Acute resp failure	52 (28.4)	47 (40.2)	0.035
Acute renal failure	2 (1.1)	6 (5.1)	0.060
Pancreatitis	2 (1.1)	4 (3.4)	0.21
Trauma	8 (4.4)	2 (1.7)	0.33
Septic shock	7 (3.8)	8 (6.8)	0.28
Other	82 (44.8)	10 (8.5)	<0.001
Presence of chronic disease	95 (51.9%)	59 (50.4%)	0.87
Alcohol	7 (3.8%)	2 (1.7%)	0.42
Multimorbidity	72 (39.3%)	40 (34.2%)	0.37
Pre-ICU service admission	135 (73.8%)	102 (87.2%)	0.005
Service admission duration, days	4.0 (13.0)	8.0 (15.0)	0.013
ICU stay duration, days	3.0 (4.0)	4.5 (8.0)	0.002
Steroid treatment	57 (31.1%)	54 (46.2%)	<0.001
Platelet Replacement	5 (2,7)	17 (14,5)	<0.001
Erythrocyte Replacement	36 (19,7)	28 (23,9)	0,055
Need for MV, at admission	15 (8.2%)	12 (10.3%)	0.15
Need for ICU MV	9 (4.9%)	51 (43.6%)	<0.001

Variables are expressed as number (%), mean ± standard deviation, and median [interquartile range]. MV: Mechanical ventilation, ICU: Intensive care unit

The entry and exit laboratory values, as well as organ function scores of patients requiring intensive care monitoring, are shown in **Table 2**. The CRP levels in the deceased group were significantly higher compared to the living group (p<0.001), however the change in CRP during ICU monitoring did not have any significance. Both the SOFA score and the APACHE score showed a significant increase in the values between admission and discharge in the deceased group, with a p-value of less than (p<0.001).

Regarding albumin values, significantly higher levels were observed in both intensive care entry and exit in the survival group. During intensive care monitoring, albumin values significantly decreased more in the deceased group (p<0.001).

The changes in CRP, albumin, SOFA score and APACHE scores during intensive care follow-up in the survival and death groups are presented in Table 3.CRP levels did not show a statistically significant difference between the survival and death groups at discharge (p=0.25 and p=0.88, respectively). Albumin levels were found to be significantly lower at the time of admission in both the survival group and the deceased group (p<0.001 for both). While the SOFA score increased significantly in the deceased group, it decreased significantly in the survival group (p<0.001 for both). APACHE score was also significantly higher in the deceased group at discharge compared to admission (p<0.001). In the survival group, however, a significant decrease in the APACHE score was observed (p<0.001).

Changes in albumin levels were found to be significantly associated with ICU mortality independent of age, sex, SOFA, and APACHE changes. Lower albumin levels were associated with worse survival (Hazard ratio: 0.80; 95% confidence interval: 0.69-0.92, p=0.001).Table 4

Table 2. Examination of laboratory values according to survival status of patients followed up in the intensive care unit

	Survival (n=183)	Deceased (n=117)	p
CRP entry	58.3(120.8)	142.5 (159.6)	<0.001
CRP exit	58.4 (92.2)	136.6 (164.5)	<0.001
CRP change	-0.32 (86.1)	9.1 (104.2)	0.31
Albumin entry	31.3 ±7.0	26.9 ±5.6	<0.001
Albumin exit	30.0±6.2	22.9 ±5.0	0.001
Albumin change	-1.3 (4.8)	-3.4 (7.1)	<0.001
SOFA entry	1.0 (1.0)	6.0 (3.0)	<0.001
SOFA exit	0.0 (1.0)	6.0 (4.59)	<0.001
SOFA change	0.0 (1.0)	3.0 (3.0)	<0.001
APACHE entry	18.0 (12.0)	29.0 (14.0)	<0.001
APACHE exit	10.0 (4.0)	55.0 (15.09	<0.001
APACHE change	-6.0 (10.0)	22.0 (16.0)	<0.001

Variables are Expressed as mean±standard Deviation and Median [interquartile range]. CRP: C-reactive protein, SOFA: Sequential Organ Failure Assessment, APACHE: Acute Physiology and Chronic Health Evaluation

Table 3. Changes of inflammatory indicators and prognostic indices upon entry and exit from intensive care unit according to survival status of patients

	Survival (n=183)			Deceased (n=117)		
	ICU entry	Exit	p	ICU entry	Exit	p
CRP	58.3(120.8)	58.4 (92.2)	0.25	142.5 (159.6)	136.6 (164.5)	088
Albumin	31.3±7.0	30.0±6.2	<0.001	26.9 ±5.6	22.9±5.0	<0.001
SOFA	1.0 (1.0)	0.0 (1.0)	<0.001	6.0 (3.0)	6.0 (4.5)	<0.001
APACHE	18.0 (12.0)	10.0 (4.0)	<0.001	29.0 (14.0)	55.0 (15.0)	<0.001

Variables are expressed as mean±standard deviation and median [interquartile range]. ICU: Intensive care unit, CRP: C-reactive protein, SOFA: Sequential organ failure assessment, APACHE: Acute Physiology and Chronic Health Evaluation

Table 4. Evaluation of risk factors affecting mortality according to survival status of patients monitored in intensive care

	Hazard ratio	95% Confidence interval	p
Age, year	1.01	0.98-1.05	0.50
Gender, male	0.41	0.08-1.70	0.20
Difference in albumin	0.80	0.69-0.92	0.001
Difference in SOFA	1.77	1.14-2.75	0.011
Difference in APACHE	1.32	1.21-1.44	<0.001

SOFA: Sequential organ failure assessment, APACHE: Acute physiology and chronic health evaluation

DISCUSSION

Albumin levels decrease in critically ill patients, both in those who survive and those who die in intensive care. A decrease in albumin levels can predict mortality independently of intensive care scoring systems and is an independent risk factor affecting mortality.

We observed a high mortality rate in patients receiving steroid treatment. Studies have shown that the use of corticosteroids is associated with infection, increased mechanical ventilation duration, and increased mortality.[10] The current findings can be attributed to the immunosuppressive effects of corticosteroids and their ability to alter infection rates. The use of corticosteroids should be closely monitored in intensive care units, and the risk-benefit ratio should be carefully reviewed.

In our study, platelet replacement was found to be significant for mortality, but the number of red blood cell replacements was deemed insignificant. In a prospective, multicenter, observational study conducted by Corwin and colleagues, the increasing number of erythrocyte transfusions received by patients was associated with longer durations of intensive care and hospital stays, as well as an increase in mortality.

It was concluded that increased number of red blood cell transfusions was an independent predictor of worse clinical outcomes.[11] The data was consistent with our study, and in a study involving 32,842 patients, intensive care unit and in-hospital platelet transfusion were not associated with increased mortality.[12]

In adults, serum albumin contributes sensitively to the regulation of osmotic pressure and vascular permeability and also contributes to physiological functions.[13] Additionally, albumin levels serve as an indicator to sensitively and effectively reflect the status of nutrition, organ function, and physical activity.[14]

Our research revealed that albumin levels were significantly associated with poor prognosis in critically ill patients. The decrease in albumin in intensive care patients can be explained by many mechanisms.

Our study demonstrated that albumin levels in critically ill patients are significantly associated with poor prognosis. The decrease in albumin levels in intensive care patients can be explained by various mechanisms. The presence of infection affects albumin balance in intensive care, particularly inflammatory processes such as sepsis, can impair vascular endothelial function, increase vascular permeability, and significantly increase systemic inflammatory factors. Increased cytokine levels can affect the gene expression and catabolism of albumin and also decrease plasma albumin concentration. This increase leads to the leakage of albumin out of the vessels, resulting in a decrease in plasma albumin levels.[15,16] The transcapillary escape of albumin is 300% in patients with septic shock and this rate increases by 100% after cardiac surgery.[17] The rate of albumin synthesis can vary significantly in critically ill patients,[17] which will exacerbate the deficit in critically ill patients.

In our study, the decrease in albumin levels was evident in both the deceased and surviving groups. This change was more pronounced in the deceased group compared to the surviving group and increased mortality. The literature supports our study. A study involving 5357 patients diagnosed with sepsis demonstrated a nonlinear relationship between albumin levels and mortality.[18] McCluskey;[19] in their study, found that serum albumin concentrations were lower in non-survivors upon admission to the intensive care unit, and serum albumin concentrations decreased more rapidly within the first 24-48 hours. In our study, albumin levels decreased in all patient groups. Kendall et al.,[20] in their study involving 577 patients, showed a strong negative trend with serum albumin levels, where survival, initially at 70.6%, decreased to 63.4% when serum albumin was ≤2.45 g/dl and further to 76.4% when the lowest serum albumin was ≤1.45 g/dl.

Studies have considered albumin levels. In a retrospective cohort study involving 18,353 patients monitored in intensive care, Jin et al.[21] found that decreasing serum albumin levels were associated with an increased risk of death. In the study, intensive care unit mortality was higher in patients with serum albumin levels <30 g/L compared to those with serum albumin levels ≥30 g/L. Serial measurement of serum albumin can provide information on the clinical prognosis of critical patients. A serum albumin level of 30 g/L has been widely accepted as the threshold and treatment target for hypoalbuminemia in clinical trials investigating the effect of albumin administration on the prognosis of critically ill patients.[22]

Despite all these data, the use of albumin in intensive care remains controversial. Serum albumin concentration will generally decrease dramatically from the early stages of a critical illness and will not usually return until the disease recovery stage, and the kinetics of administered albumin will vary greatly between critically ill patients and healthy subjects. Considering the important functions of albumin in health, it would be expected that exogenous albumin administration to increase intravascular albumin concentration would be beneficial during critical illness. However, studies have not demonstrated any benefit of albumin compared to other colloidal therapies in adults.[23] A meta-analysis reviewing 32 randomized controlled trials showed that albumin use resulted in an additional six deaths per 100 patients.[24] Recommendations by Vincent et al.[25] suggested that while the use of albumin may have a low probability of harm in most patients, it should be reserved for specific patient groups with evidence of benefit.

Limitations

The first limitation of our study is its retrospective study design, and there may be unmeasured potential confounding factors. Furthermore, the long half-life of the record also creates a limitation in terms of its marker. Therefore, when evaluating the main results of our study, it should be taken into account that the risk of type-2 error is high.

Well-designed and adequately powered controlled prospective studies are needed in the future to comprehensively identify the presence of underlying confounding factors.

CONCLUSION

We observed that albumin levels were significantly low in critically ill patients admitted to the ICU and correlated with mortality. In addition to scoring systems like APACHE II and SOFA, we believe that albumin levels could serve as an important marker. Albumin levels, being easily accessible, could be a valuable indicator in clinical monitoring and predicting mortality.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was carried out with the permission of Akdeniz University Medical Scientific Researches Ethics Committee (Date: 25.04.2024, Decision No: KAEK-274).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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